

**DATA EVALUATION RECORD
CHRONIC TOXICITY TEST WITH THE HONEY BEE
Non-Guideline Chronic Feeding Study**

1. **CHEMICAL:** Spiromesifen enol PC Code No.: 024875

2. **TEST MATERIAL:** Spiromesifen enol Purity: 99%

3. **CITATION**

Author: Tomé, H.V.V. and Porch, J.R.

Title: Spiromesifen enol- Chronic Oral Toxicity Test on the Honey Bee (*Apis mellifera* L.)

Study Completion Date: May 1, 2019

Laboratory: Eurofins EAG Agroscience, LLC

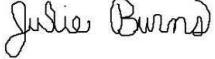
Sponsors: Bayer CropScience LP

Laboratory Report ID: 149H-110B

DP Barcode: 452560

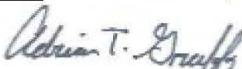
MRID No.: 50845001

4. **REVIEWED BY:** Julie Burns, Environmental Scientist, CDM/CSS-Dynamac JV


Signature:

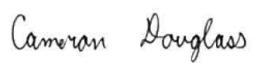
Date: 7/18/2019

APPROVED BY: Adrian Graff, Environmental Scientist, CDM/CSS-Dynamac JV


Signature:

Date: 7/22/2019

5. **APPROVED BY:** Cameron Douglass, Ph.D., Biologist, OPP/EFED/ERB IV

Signature:  2020.01.16
13:56:15 -05'00' **Date:** 01/16/2020

6. **DISCLAIMER:** *This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel. The CDM/CSS-Dynamac Joint Venture role does not include establishing Agency policies.*

7. STUDY PARAMETERS:

Test Species: *Apis mellifera* L.

Age of Test Organisms at Test Initiation: <48 hours post-emergence

Exposure Duration: 10 days

- 8. CONCLUSIONS:** Adult worker honey bees (*Apis mellifera* L.) were exposed to technical grade spiromesifen-enol (99% ai) for 10 days at the nominal dietary concentrations of 0.3, 1, 3, 10 and 30 mg ai/kg diet. Mean-measured dietary concentrations of spiromesifen-enol were 0.38, 1.2, 3.6, 11 and 33 mg ai/kg diet. Based on measured daily dietary consumption rates, and mean-measured dietary concentrations, estimated mean-measured daily doses were calculated. Estimated mean-measured daily doses of spiromesifen-enol were 0.011, 0.04, 0.12, 0.27 and 0.6 µg spiromesifen-enol/bee/day.

At the end of the 10-day exposure period, mortality was 3.3, 6.7, 0, 6.7, 13.3, 56.7 and 100%, respectively, in the negative and solvent control, and 0.011, 0.04, 0.12, 0.27 and 0.6 µg spiromesifen-enol/bee/day treatment levels. Mean food consumption was 28.2, 31, 29.8, 33.4, 33.7, 24.4 and 16.8 mg/bee/day, respectively, in the negative and solvent control, and 0.011, 0.04, 0.12, 0.27 and 0.6 µg spiromesifen-enol/bee/day treatment levels. Sublethal effects were consistently observed in the 0.27 and 0.6 (mean-measured) µg spiromesifen-enol/bee/day treatment levels, including bees that were moribund or otherwise termed as “affected” by the study author.

The NOAEL and LOAEL values for chronic exposure by adult honey bees to technical grade spiromesifen-enol (99% ai) are 0.12 and 0.27 µg spiromesifen-enol/bee/day (equivalent to 3.6 and 11 µg spiromesifen-enol/mg diet). The median lethal dose is estimated to be 0.21 µg spiromesifen-enol/bee/day (equivalent to 7.84 µg spiromesifen-enol/mg diet).

Results Synopsis

Active Ingredient	Endpoint	Dietary Concentration (µg ai/mg diet)	Daily Dietary Dose (µg ai/bee/day)
Spiromesifen enol	Mortality	LC ₅₀ : 7.84 95% C.I.: 4.04-15.9 Slope: 2.54 (1.06-4.01) NOAEC: 3.6 LOAEC: 11	LD ₅₀ : 0.21 95% C.I.: 0.1-0.4 Slope: 3.09 (0.98-5.22) NOAEL: 0.12 LOAEL: 0.27
	Food Consumption	IC ₅₀ : >33 95% C.I.: N/A Slope: N/A NOAEC: 11 LOAEC: 33	ID ₅₀ : >0.6 95% C.I.: N/A Slope: N/A NOAEL: 0.27 LOAEL: 0.6

9. ADEQUACY OF THE STUDY:

This study is scientifically sound and is classified as acceptable.

10. GUIDELINE DEVIATIONS: This study was conducted following the OECD Guideline for the Testing of Chemicals: Honey bees (*Apis mellifera* L.), chronic oral toxicity test (10 day feeding test in the laboratory). This study was reviewed according to OECD Guideline 245: Honey Bee (*Apis mellifera*) Chronic Oral Toxicity Test (10-Day Feeding), with the following deviations and deficiencies noted by reviewers:

- 1) It was not reported whether bees were kept in conditions conforming to proper cultural practices.

This deviation does not impact the acceptability of this study.

11. SUBMISSION PURPOSE: To determine the chronic effects of spiromesifen-enol on the honey bee (*A. mellifera*) for the purpose of chemical re-registration.

12. MATERIALS AND METHODS:

A. Test Organisms

Guideline Criteria	Reported Information
Species Honey Bee (<i>Apis mellifera</i> L.)	Honey bee (<i>Apis mellifera</i> L.)
Age at beginning of test Worker bees of uniform age.	Young adult worker bees, <48hrs post-emergence
Source	Test facilities' own supply (Easton, Maryland).
Were bees from diseased-free colonies?	Honey bees were from hives that had not received treatment (anti-varroa or other pathogens) within four weeks of the test. Colonies were apparently healthy and queen-right.
Were bees kept in conditions	Not reported.

Guideline Criteria	Reported Information
conforming to proper cultural practices?	
<u>Acclimation conditions</u>	About 24 hours prior to test start, bees were placed in test chambers under red light (without immobilization) and acclimated in darkness. Bees were held in an incubator maintained at 33°C with 63-66% relative humidity, and fed 50% (w/v) sucrose solution <i>ad libitum</i> .

B. Test System

Guideline Criteria	Reported Information
<u>Test Chambers</u>	Perforated, stainless steel cylinders (diameter: 9cm, height: 9cm). Test chambers were covered with petri dishes lined with filter paper.
<u>Temperature during exposure</u>	Average of 33°C
<u>Relative humidity during exposure</u>	Average of 59%
<u>Lighting</u>	Bees maintained in darkness, except during dosing and observations.
<u>Feeding</u>	Bees were fed treated 50% sucrose solution in acetone (exposed groups), untreated 50% sucrose solution (negative control), or untreated 50% sucrose solution in acetone (solvent control). Bees were fed <i>ad libitum</i> with syringes that were renewed daily.

C. Test Design

Guideline Criteria	Reported Information
<u>Test material</u>	<p>Identity: Spiromesifen/AE 0952850 Synonyms: BSN2060-enol IUPAC name: 4-hydroxy-3-(2,4,6-trimethylphenyl)-1-oxaspiro[4,4]non-3-en-2-one CAS No.: 148476-30-6 Batch ID: AE 0920586 00 1B99 0001 Purity: 99.0% Storage: 5 ± 5°C</p>
<u>Nominal application rates</u> The test material should be applied at the maximum proposed label rate.	<p><u>Diet concentrations:</u> 0 (negative and solvent controls), 0.30, 1.0, 3.0, 10, and 30 mg ai/kg diet</p> <p><u>Actual intake dietary doses:</u> Not reported.</p>
<u>Dose Preparation</u>	<p>Stock solutions and subsequent dilutions for each treatment group were prepared fresh daily. The primary stock solution was prepared by bringing 0.1788 g of spiromesifen enol to a volume of 50 mL with acetone. A secondary stock solution was prepared by dilution of the primary, by bringing a 16.7 mL aliquot to a final volume of 50 mL with acetone. Three additional stock solutions were prepared from dilutions of this solution with acetone. Diet solutions were prepared using serial dilutions of the appropriate stock solutions using 50% aqueous sucrose solution to make each treatment concentration. All solutions were mixed by inverting and appeared clear and colorless with no visible particulates.</p>
<u>Number of bees exposed</u>	<p>Each treatment (including untreated control, vehicle control, and toxic</p>

Guideline Criteria	Reported Information
	reference item) had 3 replicates, with 10 bees per replicate. 30 total bees per treatment application were exposed.
<u>Application methods</u>	<p>The test sucrose feeding solutions were provided <i>ad libitum</i> with two syringe feeders inserted through the lid of the test chamber. Feeders were renewed every day with ~2.5 mL of freshly prepared treatment solutions.</p> <p>Feeders were weighed before and after feeding. The food consumed was determined by comparing the initial and remaining weights.</p>
<u>Other experimental design information</u>	Individual daily consumption was corrected for daily mortality and for estimated evaporation. Three additional test cages containing syringes filled with 50% aqueous sucrose solution but without bees were set up and syringes were weighed daily to estimate evaporation.
<u>Were bees randomly or impartially assigned to test groups?</u>	Yes, test cages were impartially allocated to the treatment and control groups.
<u>Control(s)</u>	<p>Negative control: 50% aqueous sucrose solution</p> <p>Solvent Control: 50% aqueous sucrose solution + acetone</p>
<u>Exposure period</u>	10 days
<u>Positive Control, (if any)</u>	Toxic reference item: Dimethoate (0.65 mg ai/kg diet)

13. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	<p>Yes. This study was conducted in compliance with the EPA GLP Standards specified under FIFRA and as accepted by the OECD Principles of Good Laboratory Practice with the following exceptions:</p> <ol style="list-style-type: none"> 1) Periodic analyses of water and sugar for potential contaminants were not performed in accordance with GLP. 2) The stability, homogeneity, and verification of the reference item in the dose solutions were not determined in accordance with GLP. 3) The characterization and stability of the reference substance under the conditions of storage at the site were not determined in compliance with GLP.
<u>Control mortality</u>	<p>3% mortality was observed in the negative control, and 7% mortality was observed in the solvent control at test termination.</p>
Were raw data included?	<p>Yes.</p>
Were signs of toxicity (if any) described?	<p>Affected bees were observed every 24 hours (within the first four hours of dosing), at all treatment levels for abnormalities such as apathy, affected, cramps, vomiting, etc.</p>

Mortality and Observations:

At the end of the 10-day exposure period, mortality was 3, 7, 0, 7, 13, 57 and 100%, respectively,

in the negative and solvent control, and 0.011, 0.04, 0.12, 0.27 and 0.6 (mean-measured) µg spiromesifen-enol/bee/day treatment levels (**Table 1**). Mortality in the reference item treatment level (0.013 µg dimethoate/bee/day) was 100%.

Sublethal effects were consistently observed in the 0.27 and 0.6 (mean-measured) µg spiromesifen-enol/bee/day treatment levels, including bees that were moribund or otherwise termed as “affected” by the study author.

Table 1. Study Author-Reported Data on Cumulative Adult Honey bee Mortality After Repeated Exposure to TG Spiromesifen-enol (99% ai).

Mean-measured Daily Dose (μg spiromesifen/bee/day)	Number Exposed	% Mortality at Day 10	Behavioral Abnormalities
Negative Control	30	3	None
Solvent Control	30	7	None
0.011	30	0	None
0.04	30	7	1 moribund D9
0.12	30	13	None
0.27	30	57*	1 affected D6 & D7, 1 moribund D9
0.6	30	100*	1 moribund D3, 1 affected D4 & D5
Dimethoate			
0.012	30	100	

* Per the study author, treatment mean is significantly ($p < 0.05$) different from the solvent control treatment mean according to a Williams test.

Study Author's Statistical Analysis

The study author's statistical analyses relied on CETIS statistical software (ver. 1.9.1), and used mean-measured dietary concentrations and estimated mean-measured dietary doses based on measured food consumption.

The Williams Test was used to compare mortality in treatment groups with that in the negative control. Regression analyses were conducted using Probit analysis.

10-day LC₅₀: 0.24 µg spiromesifen-enol/bee/d 95% C.I.: 0.12-0.35 µg ai/bee/d
NOAEC: 0.12 µg spiromesifen-enol/bee/d

Reviewer's Statistical Verification:

At the end of the 10-day exposure period, mean food consumption was 28.2, 29.8, 33.4, 33.7, 24.4 and 16.8 mg/bee/day, respectively, in the negative control, 0.011, 0.04, 0.12, 0.27 and 0.6 (mean-measured) µg spiromesifen-enol/bee/day treatment levels (**Table 2**).

Table 2. Reviewer-Calculated Data on Cumulative Adult Honey bee Mortality and Food Consumption After Repeated Exposure to TG Spiromesifen-enol (99% ai).

Mean-measured Daily Dose (µg spiromesifen/bee/day)	D 10 Mortality (% of Negative Control)	Food Consumption (% of Negative Control)
0.011	+3.5	+5.7
0.04	-3.5	+18.1
0.12	-10.3	+19.1
0.27	-55.2 ¶	-13.8
0.6	-100 ¶	-40.6 †

† Treatment mean is significantly ($p < 0.05$) different from the untreated control treatment mean according to a Dunnett's test.

¶ Treatment mean is significantly ($p < 0.05$) different from the untreated control treatment mean according to a Jonckheere-Terpstra's Step-Down test.

The reviewer analyzed mortality and food consumption data using CETIS statistical software version 1.9.5.3 with database backend settings implemented by EFED on 7/25/17. For spiromesifen-enol residues, measured dietary concentrations, and estimated measured dietary doses were used for analyses.

The negative and solvent control treatment means were compared using an Equal Variance t Two-Sample test ($\alpha = 0.05$). There were no significant differences between the control treatment means and so all statistical comparisons were made relative to the negative control.

Data were tested for normality using Shapiro-Wilk's test and for homogeneity of variance using the modified Levene Equality of Variance Test ($\alpha = 0.01$). Food consumption data met assumptions for parametric testing, and so Analysis of Variance (ANOVA) and Dunnett's test ($\alpha = 0.05$) were used to compare mortality treatment means to the untreated control treatment mean. On the other hand, mortality data did not meet assumptions for parametric testing, and so Analysis of Variance (ANOVA) and Jonckheere Terpstra's Step Down test ($\alpha = 0.05$) were used to compare mortality treatment means to the untreated control treatment mean. Hypothesis testing was conducted on the basis of spiromesifen-enol measured dietary concentrations, and then these mean comparison results applied to estimated mean-measured daily doses.

The LD₅₀ values were estimated using linear regression (log-normal/Probit); IC₅₀ values based on food consumption were not statistically evaluated because the maximum inhibition was <50%.

Results Synopsis

Active Ingredient	Endpoint	Dietary Concentration ($\mu\text{g ai/mg diet}$)	Daily Dietary Dose ($\mu\text{g ai/bee/day}$)
Spiromesifen enol	Mortality	LC ₅₀ : 7.84 95% C.I.: 4.04-15.9 Slope: 2.54 (1.06-4.01) NOAEC: 3.6 LOAEC: 11	LD ₅₀ : 0.21 95% C.I.: 0.1-0.4 Slope: 3.09 (0.98-5.22) NOAEL: 0.12 LOAEL: 0.27
	Food Consumption	IC ₅₀ : >33 95% C.I.: N/A Slope: N/A NOAEC: 11 LOAEC: 33	ID ₅₀ : >0.6 95% C.I.: N/A Slope: N/A NOAEL: 0.27 LOAEL: 0.6

14. REVIEWER'S COMMENTS:

The in-life phase of this study was conducted from February 19 to March 1, 2019. Validity criteria specified in OECD Guideline 245 appear to have been met, specifically: 1) average control mortality was $\leq 15\%$ by test termination; and 2) average reference item mortality was $\geq 50\%$ by test termination.

The reviewer's results and those of the study author agreed with regards to the determination of the NOAEC/L value, in spite of slightly different approaches to statistically deriving this endpoint. However, the reviewer's LD₅₀ values were lower than those calculated by the study author, which can be attributed to the reviewer using linear regression while the study author used Probit regression models. Also, the reviewer additionally analyzed food consumption data for spiromesifen enol. The reviewer's results are reported in the Executive Summary and Conclusions sections of this DER.

The nominal actual intake dietary doses were calculated by the study author using daily diet consumption, daily evaporative loss, and daily mortality.

15. REFERENCES:

1. European Food Safety Authority. 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. And Solitary Bees). EFSA Journal 2013: 11(7)3295, 266pp.
2. French Association for Plant Protection. 2003. Methods Used to Assess the Effects of Crop Protection Products on Honeybees, *Apis mellifera* L. Biological Tests Committee Method no. 230, 1st version: November 2003.

DP Barcode: 452560

MRID No.: 50845001

3. Tidepool Scientific Software. 2011. *Users Guide, Comprehensive Environmental Toxicity Information System (CETIS)*. Tidepool Scientific Software, McKinleyville, CA.

All other references pertain to standard guidance or methods.

CETIS Summary Report

Report Date: 17 Jul-19 16:12 (p 1 of 2)

Test Code/ID: 50845001 dd / 07-3139-5452

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study**Eurofins EAG Agroscience LLC**

Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
Sample ID:	18-7807-4334	Code:	50845001 dd	Age:	
Sample Date:	19 Feb-19	Material:	Spiromesifen-enol	Project:	Insecticide
Receipt Date:		CAS (PC):		Source:	Bayer CropScience
Sample Age:	n/a	Client:	CDM Smith	Station:	

024875 50845001 measured dd; Record Created by: J. Burns

Single Comparison Summary

Analysis ID	Endpoint	Comparison Method	P-Value	Comparison Result			\$
17-4305-7742	10-Day Mortality Rate	Equal Variance t Two-Sample Test	0.6779	Solvent Blank passed	10-day mortality rate	1	
17-1182-9653	Food Consumption	Equal Variance t Two-Sample Test	0.2704	Solvent Blank passed	food consumption	1	

Multiple Comparison Summary

Analysis ID	Endpoint	Comparison Method	✓ NOEL	LOEL	TOEL	TU	PMSD	\$
04-7455-0980	10-Day Mortality Rate	Jonckheere-Terpstra Step-Down Test	✓ 0.12	0.27	0.18		n/a	1
09-2782-2734	10-Day Mortality Rate	Mann-Whitney U Two-Sample Test	0.27	0.6	0.4025		39.8%	1
03-1466-0401	Food Consumption	Dunnett Multiple Comparison Test	0.27	0.6	0.4025		33.1%	1
19-2954-1114	Food Consumption	Williams Multiple Comparison Test	0.27	0.6	0.4025		25.5%	1

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓ Level	ug/bee/day	95% LCL	95% UCL	TU	\$
17-1326-1333	10-Day Mortality Rate	GLM: Log-Normal (Probit)	✓ EC5	0.0607	0.0035	0.116		1
			✓ EC10	0.0795	0.00798	0.14		
			✓ EC25	0.125	0.03	0.204		
			✓ EC50	0.206	0.103	0.397		
12-8218-8541	10-Day Mortality Rate	Spearman-Kärber	EC50	0.216	0.175	0.265		1
02-7253-2663	Food Consumption	NLR: 3P Cum Log-Normal (Probit)	EC5	0.153	n/a	0.282		1
			EC10	0.209	n/a	0.36		
			EC25	0.352	0.199	0.516		
			EC50	0.628	0.403	0.976		

10-Day Mortality Rate Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	S	3	0.067	0.000	0.354	0.000	0.200	0.067	0.115	173.21%	0.00%
0	N	3	0.033	0.000	0.177	0.000	0.100	0.033	0.058	173.21%	-3.57%
0.011		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-7.14%
0.04		3	0.067	0.000	0.354	0.000	0.200	0.067	0.115	173.21%	0.00%
0.12		3	0.133	0.000	0.420	0.000	0.200	0.067	0.115	86.60%	7.14%
0.27		3	0.567	0.000	1.000	0.000	1.000	0.296	0.513	90.56%	53.57%
0.6		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%

Food Consumption Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	S	3	31	22.8	39.2	27.4	34	1.91	3.3	10.67%	0.00%
0	N	3	28.2	24.2	32.3	26.8	30	0.935	1.62	5.73%	8.76%
0.011		3	29.8	21.2	38.5	27.1	33.8	2	3.47	11.63%	3.59%
0.04		3	33.4	14.5	52.2	24.8	39.3	4.39	7.6	22.77%	-7.78%
0.12		3	33.7	18.3	49	27	39.2	3.56	6.16	18.31%	-8.70%
0.27		3	24.4	17.9	30.8	22.4	27.3	1.51	2.61	10.72%	21.32%
0.6		3	16.8	9.49	24.1	13.5	19.2	1.7	2.94	17.52%	45.76%

CETIS Summary ReportReport Date: 17 Jul-19 16:12 (p 2 of 2)
Test Code/ID: 50845001 dd / 07-3139-5452**Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study****Eurofins EAG Agroscience LLC****10-Day Mortality Rate Detail**

Conc-ug/bee/day	Code	Rep 1	Rep 2	Rep 3
0	S	0.000	0.200	0.000
0	N	0.000	0.100	0.000
0.011		0.000	0.000	0.000
0.04		0.000	0.200	0.000
0.12		0.200	0.000	0.200
0.27		0.000	1.000	0.700
0.6		1.000	1.000	1.000

Food Consumption Detail

Conc-ug/bee/day	Code	Rep 1	Rep 2	Rep 3
0	S	31.5	34	27.4
0	N	26.8	28	30
0.011		33.8	27.1	28.7
0.04		24.8	36	39.3
0.12		39.2	27	34.7
0.27		22.4	23.3	27.3
0.6		19.2	17.7	13.5

CETIS Summary Report

Report Date: 17 Jul-19 16:15 (p 1 of 2)

Test Code/ID: 50845001 dc / 09-7178-1966

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study**Eurofins EAG Agroscience LLC**

Batch ID:	09-1432-1139	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
Sample ID:	16-2105-3269	Code:	50845001 dc	Age:	
Sample Date:	19 Feb-19	Material:	Spiromesifen-enol	Project:	Insecticide
Receipt Date:	17 Jul-19 16:01	CAS (PC):		Source:	Bayer CropScience
Sample Age:	n/a	Client:	CDM Smith	Station:	

024875 50845001 measured dc, Record created by: J. Burns; Cetis Comments: 'Food Consumption' endpoint...

3P Cum Log-Normal (Probit) Model: The chosen model failed to converge, therefore Ecp/lcp estimates will not be calculated. Try selecting a different another model, changing the starting parameters or parameter constraints, or increase the maximum number of iterations. Important: A primary reason for failure to converge is poor model specification, ill-conditioned matrices or collinearity. The pseudo Hessian matrix condition number (ratio of highest eigenvalue to lowest eigenvalue) for this data set is 6.

Multiple Comparison Summary

Analysis ID	Endpoint	Comparison Method	✓ NOEL	LOEL	TOEL	TU	PMSD	S
09-1395-7295	10-Day Mortality Rate	Jonckheere-Terpstra Step-Down Test	✓ 3.6	11	6.293		n/a	1
09-9443-6799	10-Day Mortality Rate	Mann-Whitney U Two-Sample Test	11	33	19.05		39.8%	1
13-1701-1735	Food Consumption	Dunnett Multiple Comparison Test	11	33	19.05		33.1%	1
01-1870-0748	Food Consumption	Williams Multiple Comparison Test	11	33	19.05		25.5%	1

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓ Level	mg ai/kg	95% LCL	95% UCL	TU	S
04-1832-4856	10-Day Mortality Rate	GLM: Log-Normal (Probit)	EC5	1.76	0.194	3.57		1
			EC10	2.45	0.411	4.59		
			EC25	4.25	1.35	7.42		
			✓ EC50	7.84	4.04	15.9		
21-3477-9190	10-Day Mortality Rate	Spearman-Kärber	EC50	8.49	6.57	11		1

10-Day Mortality Rate Summary

Conc-mg ai/kg	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	S	3	0.067	0.000	0.354	0.000	0.200	0.067	0.115	173.21%	0.00%
0	N	3	0.033	0.000	0.177	0.000	0.100	0.033	0.058	173.21%	-3.57%
0.38		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-7.14%
1.2		3	0.067	0.000	0.354	0.000	0.200	0.067	0.115	173.21%	0.00%
3.6		3	0.133	0.000	0.420	0.000	0.200	0.067	0.115	86.60%	7.14%
11		3	0.567	0.000	1.000	0.000	1.000	0.296	0.513	90.56%	53.57%
33		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%

Food Consumption Summary

Conc-mg ai/kg	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	S	3	31	22.8	39.2	27.4	34	1.91	3.3	10.67%	0.00%
0	N	3	28.2	24.2	32.3	26.8	30	0.935	1.62	5.73%	8.76%
0.38		3	29.8	21.2	38.5	27.1	33.8	2	3.47	11.63%	3.59%
1.2		3	33.4	14.5	52.2	24.8	39.3	4.39	7.6	22.77%	-7.78%
3.6		3	33.7	18.3	49	27	39.2	3.56	6.16	18.31%	-8.70%
11		3	24.4	17.9	30.8	22.4	27.3	1.51	2.61	10.72%	21.32%
33		3	16.8	9.49	24.1	13.5	19.2	1.7	2.94	17.52%	45.76%

CETIS Summary Report

Report Date: 17 Jul-19 16:15 (p 2 of 2)
Test Code/ID: 50845001 dc / 09-7178-1966

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study**Eurofins EAG Agroscience LLC****10-Day Mortality Rate Detail**

Conc-mg ai/kg	Code	Rep 1	Rep 2	Rep 3
0	S	0.000	0.200	0.000
0	N	0.000	0.100	0.000
0.38		0.000	0.000	0.000
1.2		0.000	0.200	0.000
3.6		0.200	0.000	0.200
11		0.000	1.000	0.700
33		1.000	1.000	1.000

Food Consumption Detail

Conc-mg ai/kg	Code	Rep 1	Rep 2	Rep 3
0	S	31.5	34	27.4
0	N	26.8	28	30
0.38		33.8	27.1	28.7
1.2		24.8	36	39.3
3.6		39.2	27	34.7
11		22.4	23.3	27.3
33		19.2	17.7	13.5

CETIS Analytical Report

Report Date: 17 Jul-19 16:10 (p 1 of 6)
 Test Code/ID: 50845001 dd / 07-3139-5452

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

Eurofins EAG Agroscience LLC

Analysis ID:	17-4305-7742	Endpoint:	10-Day Mortality Rate	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 15:56	Analysis:	Parametric-Two Sample	Status Level:	1

Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
				Age:	

Data Transform	Alt Hyp	Comparison Result	PMSD
Untransformed	C <> T	Solvent Blank passed 10-day mortality rate	21.41%

Equal Variance t Two-Sample Test

Control	vs	Control II	Test Stat	Critical	MSD	DF	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control		Solvent Blank	0.447	2.78	0.207	4	CDF	0.6779	Non-Significant Effect

ANOVA Table

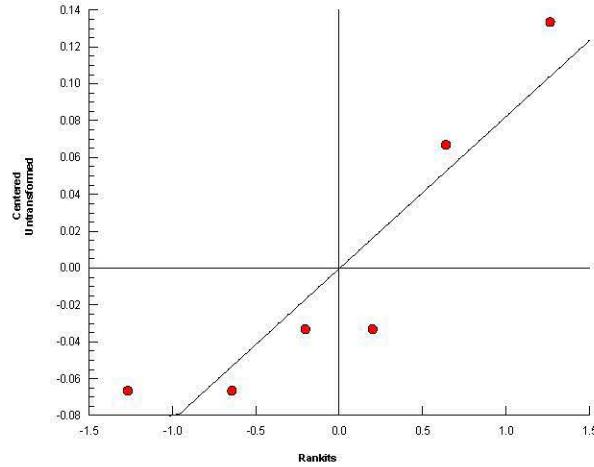
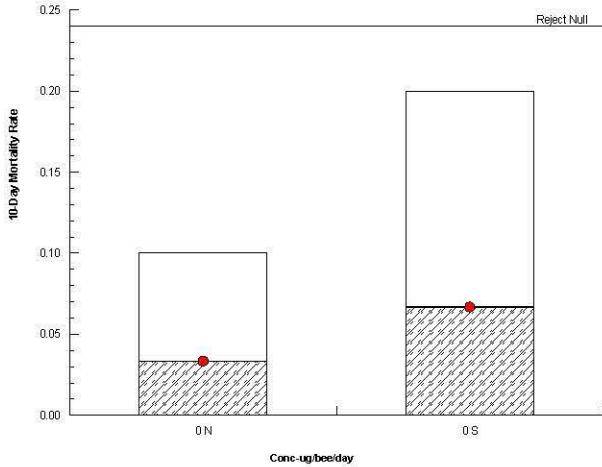
Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Between	0.00166667	0.00166667	1	0.2	0.6779	Non-Significant Effect
Error	0.03333333	0.00833333	4			
Total	0.035		5			

ANOVA Assumptions Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:1\%$)
Variance	Variance Ratio F Test	4	199	0.4000	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.827	0.43	0.1012	Normal Distribution

10-Day Mortality Rate Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	S	3	0.067	0.000	0.354	0.000	0.000	0.200	0.067	173.21%	0.00%
0	N	3	0.033	0.000	0.177	0.000	0.000	0.100	0.033	173.21%	-3.57%

Graphics

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study				Eurofins EAG Agroscience LLC			
Analysis ID: 09-2782-2734	Endpoint: 10-Day Mortality Rate		CETIS Version: CETISv1.9.5				
Analyzed: 17 Jul-19 15:57	Analysis: Nonparametric-Two Sample		Status Level: 1				
Batch ID: 16-7140-8845	Test Type: 2014 Honeybee Adult Chron Oral		Analyst:				
Start Date: 19 Feb-19	Protocol: Honeybee Adult Chronic Oral Toxicity, 10-d		Diluent:				
Ending Date: 01 Mar-19	Species: Apis mellifera		Brine:				
Test Length: 10d 0h	Taxon:		Source: Eurofins Agroscience Servi	Age:			
Data Transform	Alt Hyp		NOEL	LOEL	TOEL	TU	PMSD
Untransformed	C < T		0.27	0.6	0.4025		39.81%

Mann-Whitney U Two-Sample Test

Control	vs	Conc-ug/bee/day	Test Stat	Critical	Ties	DF	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control	0.011	3	n/a	1	4	Exact	1.0000	Non-Significant Effect	
	0.04	5	n/a	1	4	Exact	0.5000	Non-Significant Effect	
	0.12	7	n/a	1	4	Exact	0.2000	Non-Significant Effect	
	0.27	7	n/a	1	4	Exact	0.2000	Non-Significant Effect	
	0.6*	9	n/a	0	4	Exact	0.0500	Significant Effect	

ANOVA Table

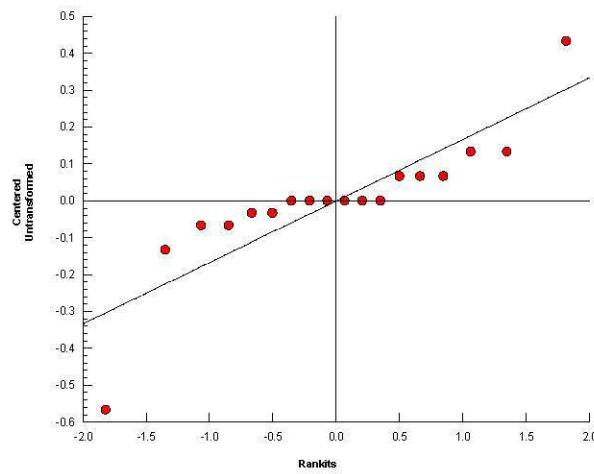
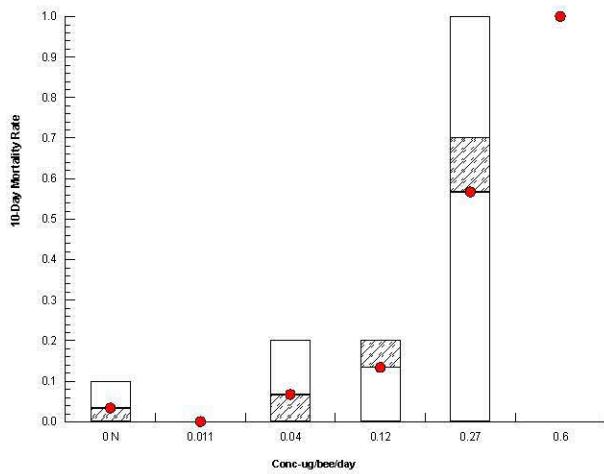
Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Between	2.41333	0.482667	5	9.87	6.2E-04	Significant Effect
Error	0.586667	0.0488889	12			
Total	3		17			

ANOVA Assumptions Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:1\%$)
Variance	Levene Equality of Variance Test	6.88	5.06	0.0030	Unequal Variances
	Mod Levene Equality of Variance Test	3.43	8.75	0.0826	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.791	0.855	0.0011	Non-Normal Distribution

10-Day Mortality Rate Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	N	3	0.033	0.000	0.177	0.000	0.000	0.100	0.033	173.21%	0.00%
0.011		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-3.45%
0.04		3	0.067	0.000	0.354	0.000	0.000	0.200	0.067	173.21%	3.45%
0.12		3	0.133	0.000	0.420	0.200	0.000	0.200	0.067	86.60%	10.34%
0.27		3	0.567	0.000	1.000	0.700	0.000	1.000	0.296	90.56%	55.17%
0.6		3	1.000	1.000	1.000	1.000	1.000	1.000	0.000	0.00%	100.00%

Graphics

CETIS Analytical Report

Report Date: 17 Jul-19 16:10 (p 3 of 6)
 Test Code/ID: 50845001 dd / 07-3139-5452

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study				Eurofins EAG Agroscience LLC			
Analysis ID:	04-7455-0980	Endpoint:	10-Day Mortality Rate	CETIS Version:	CETISv1.9.5		
Analyzed:	17 Jul-19 15:57	Analysis:	Nonparametric-Control vs Ord. Treatments	Status Level:	1		
Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:			
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:			
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:			
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi		
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU
Untransformed	C < T			0.12	0.27	0.18	

Jonckheere-Terpstra Step-Down Test

Control	vs	Conc-ug/bee/day	Test Stat	Critical	Ties	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control		0.011	-1	1.64	1	Asymp	0.8413	Non-Significant Effect
		0.04	0.153	1.64	1	Asymp	0.4392	Non-Significant Effect
		0.12	1.29	1.64	2	Asymp	0.0986	Non-Significant Effect
		0.27*	2.02	1.64	2	Asymp	0.0217	Significant Effect
		0.6*	3.21	1.64	3	Asymp	6.7E-04	Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Between	2.41333	0.482667	5	9.87	6.2E-04	Significant Effect
Error	0.586667	0.0488889	12			
Total	3		17			

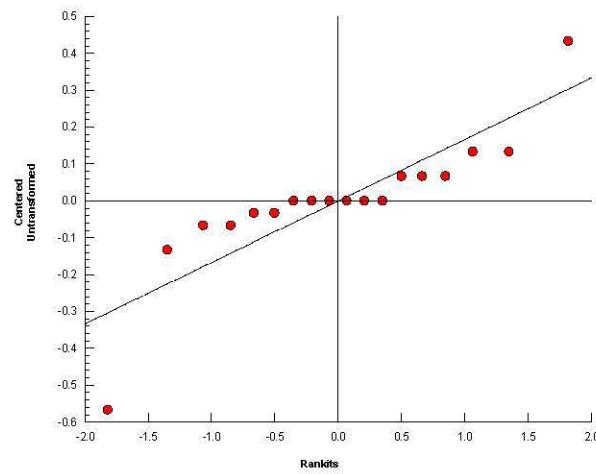
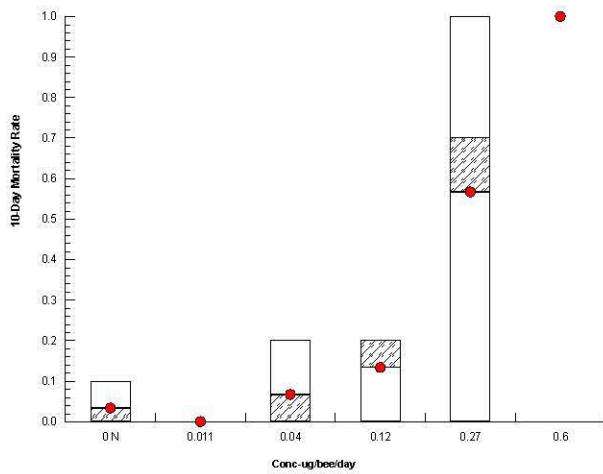
ANOVA Assumptions Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:1\%$)
Variance	Levene Equality of Variance Test	6.88	5.06	0.0030	Unequal Variances
	Mod Levene Equality of Variance Test	3.43	8.75	0.0826	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.791	0.855	0.0011	Non-Normal Distribution

10-Day Mortality Rate Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	N	3	0.033	0.000	0.177	0.000	0.000	0.100	0.033	173.21%	0.00%
0.011		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-3.45%
0.04		3	0.067	0.000	0.354	0.000	0.000	0.200	0.067	173.21%	3.45%
0.12		3	0.133	0.000	0.420	0.200	0.000	0.200	0.067	86.60%	10.34%
0.27		3	0.567	0.000	1.000	0.700	0.000	1.000	0.296	90.56%	55.17%
0.6		3	1.000	1.000	1.000	1.000	1.000	1.000	0.000	0.00%	100.00%

Graphics



Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study Eurofins EAG Agroscience LLC

Analysis ID:	17-1182-9653	Endpoint:	Food Consumption	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 15:56	Analysis:	Parametric-Two Sample	Status Level:	1

Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:
Test Length:	10d 0h	Taxon:		Source: Eurofins Agroscience Servi Age:

Data Transform	Alt Hyp	Comparison Result	PMSD
Untransformed	C < T	Solvent Blank passed food consumption	20.87%

Equal Variance t Two-Sample Test

Control	vs	Control II	Test Stat	Critical	MSD	DF	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control		Solvent Blank	1.28	2.78	5.9	4	CDF	0.2704	Non-Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Between	11.0433	11.0433	1	1.63	0.2704	Non-Significant Effect
Error	27.0547	6.76367	4			
Total	38.0979		5			

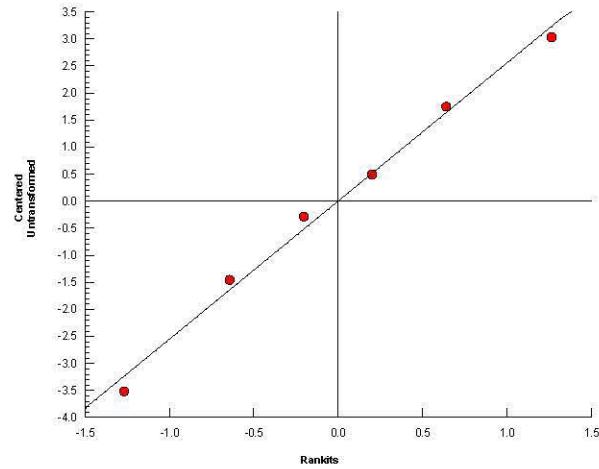
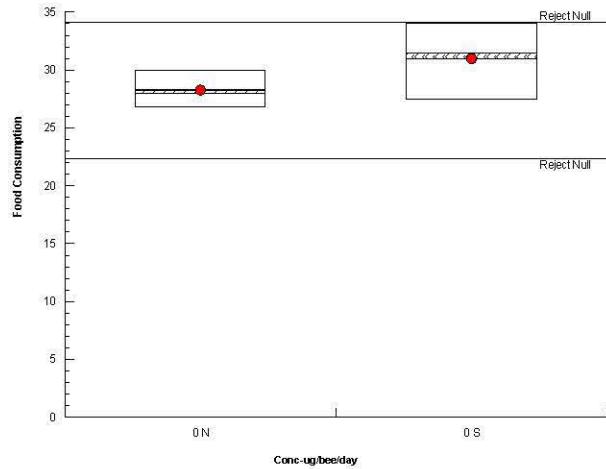
ANOVA Assumptions Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:1\%$)
Variance	Variance Ratio F Test	4.16	199	0.3876	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.991	0.43	0.9917	Normal Distribution

Food Consumption Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	S	3	31	22.8	39.2	31.4	27.4	34	1.91	10.67%	0.00%
0	N	3	28.2	24.2	32.3	28	26.8	30	0.935	5.73%	8.76%

Graphics



Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study				Eurofins EAG Agroscience LLC				
Analysis ID:	03-1466-0401	Endpoint:	Food Consumption	CETIS Version:	CETISv1.9.5			
Analyzed:	17 Jul-19 15:57	Analysis:	Parametric-Control vs Treatments	Status Level:	1			
Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:				
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:				
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:				
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi			
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU	PMSD
Untransformed	C > T			0.27	0.6	0.4025		33.12%

Dunnett Multiple Comparison Test

Control	vs	Conc-ug/bee/	Test Stat	Critical	MSD	DF	P-Type	P-Value	Decision(α :5%)
Negative Control	0.011		-0.429	2.5	9.36	4	CDF	0.9283	Non-Significant Effect
	0.04		-1.37	2.5	9.36	4	CDF	0.9930	Non-Significant Effect
	0.12		-1.45	2.5	9.36	4	CDF	0.9943	Non-Significant Effect
	0.27		1.04	2.5	9.36	4	CDF	0.4087	Non-Significant Effect
	0.6*		3.06	2.5	9.36	4	CDF	0.0188	Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α :5%)
Between	607.867	121.574	5	5.8	0.0060	Significant Effect
Error	251.645	20.9705	12			
Total	859.513		17			

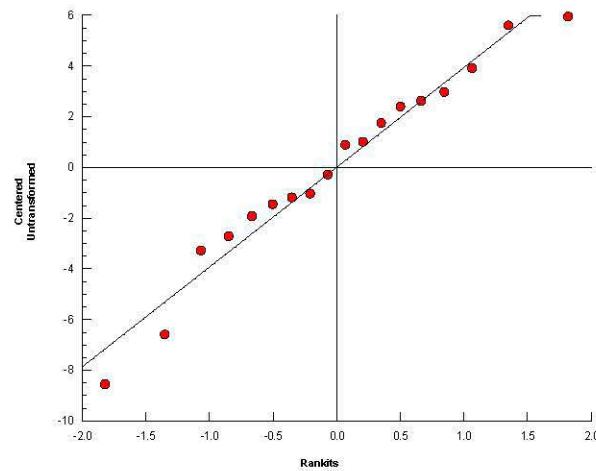
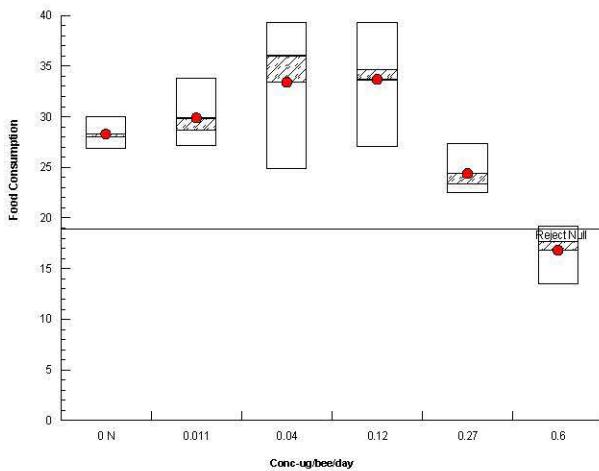
ANOVA Assumptions Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α :1%)
Variance	Bartlett Equality of Variance Test	5.08	15.1	0.4057	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.966	0.855	0.7260	Normal Distribution

Food Consumption Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	N	3	28.2	24.2	32.3	28	26.8	30	0.935	5.73%	0.00%
0.011		3	29.8	21.2	38.5	28.7	27.1	33.8	2	11.63%	-5.68%
0.04		3	33.4	14.5	52.2	36	24.8	39.3	4.39	22.77%	-18.14%
0.12		3	33.7	18.3	49	34.7	27	39.2	3.56	18.31%	-19.14%
0.27		3	24.4	17.9	30.8	23.3	22.4	27.3	1.51	10.72%	13.76%
0.6		3	16.8	9.49	24.1	17.7	13.5	19.2	1.7	17.52%	40.55%

Graphics



Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study				Eurofins EAG Agroscience LLC				
Analysis ID:	19-2954-1114	Endpoint:	Food Consumption	CETIS Version:	CETISv1.9.5			
Analyzed:	17 Jul-19 15:58	Analysis:	Parametric-Control vs Ord.Treatments	Status Level:	1			
Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:				
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:				
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:				
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi			
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU	PMSD
Untransformed	C > T			0.27	0.6	0.4025		25.51%

Williams Multiple Comparison Test

Control	vs	Conc-ug/bee/	Test Stat	Critical	MSD	DF	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control	0.011		-0.429	1.78	6.66	4	CDF	>0.05	Non-Significant Effect
	0.04		-0.9	1.87	7	4	CDF	>0.05	Non-Significant Effect
	0.12		-1.08	1.9	7.12	4	CDF	>0.05	Non-Significant Effect
	0.27		1.04	1.92	7.17	4	CDF	>0.05	Non-Significant Effect
	0.6*		3.06	1.93	7.21	4	CDF	<0.05	Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Between	607.867	121.574	5	5.8	0.0060	Significant Effect
Error	251.645	20.9705	12			
Total	859.513		17			

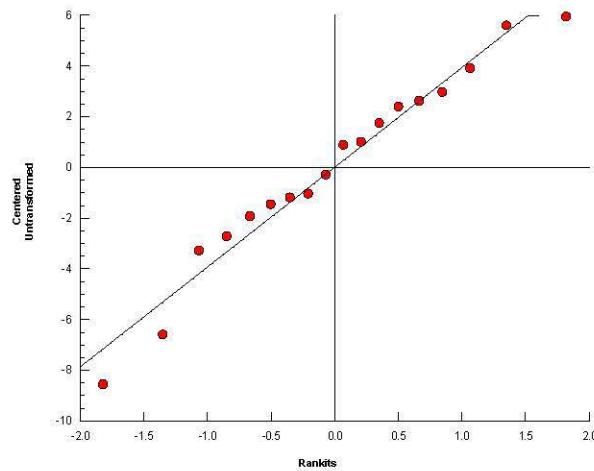
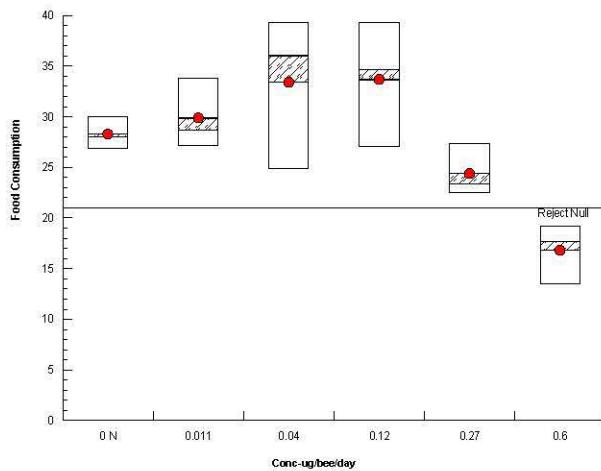
ANOVA Assumptions Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:1\%$)
Variance	Bartlett Equality of Variance Test	5.08	15.1	0.4057	Equal Variances
Distribution	Shapiro-Wilk W Normality Test	0.966	0.855	0.7260	Normal Distribution

Food Consumption Summary

Conc-ug/bee/day	Code	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	N	3	28.2	24.2	32.3	28	26.8	30	0.935	5.73%	0.00%
0.011		3	29.8	21.2	38.5	28.7	27.1	33.8	2	11.63%	-5.68%
0.04		3	33.4	14.5	52.2	36	24.8	39.3	4.39	22.77%	-18.14%
0.12		3	33.7	18.3	49	34.7	27	39.2	3.56	18.31%	-19.14%
0.27		3	24.4	17.9	30.8	23.3	22.4	27.3	1.51	10.72%	13.76%
0.6		3	16.8	9.49	24.1	17.7	13.5	19.2	1.7	17.52%	40.55%

Graphics



CETIS Analytical Report

Report Date: 17 Jul-19 16:11 (p 1 of 2)
 Test Code/ID: 50845001 dd / 07-3139-5452

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study				Eurofins EAG Agroscience LLC	
Analysis ID:	17-1326-1333	Endpoint:	10-Day Mortality Rate	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 15:57	Analysis:	Linear Regression (GLM)	Status Level:	1
Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
Age:					

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSE	F Stat	P-Value	Decision($\alpha:5\%$)
8	-28.7	62.4	62.9	-0.685	0.323	1		0.837	0.5040	Non-Significant Lack of Fit

Point Estimates

Level	ug/bee/day	95% LCL	95% UCL
EC5	0.0607	0.0035	0.116
EC10	0.0795	0.00798	0.14
EC25	0.125	0.03	0.204
EC50	0.206	0.103	0.397

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	2.12	0.729	0.546	3.7	2.91	0.0122	Significant Parameter
Slope	3.09	0.982	0.974	5.22	3.15	0.0076	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	572000	572000	1	135000	<1.0E-37	Significant
Lack of Fit	11.1	3.69	3	0.837	0.5039	Non-Significant
Pure Error	44.1	4.41	10			
Residual	55.2	4.24	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	47.6	22.4	7.6E-06	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	55.2	22.4	4.2E-07	Significant Heterogeneity
Variance	Mod Levene Equality of Variance	1.25	5.19	0.3987	Equal Variances
	Anderson-Darling A2 Normality Test	1.09	2.49	0.0074	Non-Normal Distribution
Distribution	Shapiro-Wilk W Normality Test	0.878	0.882	0.0445	Non-Normal Distribution
	Tarone C(α) Binomial Overdispersion	7.94	1.64	<1.0E-37	Significant Overdispersion

10-Day Mortality Rate Summary**Calculated Variate(A/B)**

Conc-ug/bee/day	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.011		3	0.000	0.000	0.000	0.000	0.000	0.0%	0	30	
0.04		3	0.067	0.000	0.200	0.067	0.115	173.00%	6.67%	2	30
0.12		3	0.133	0.000	0.200	0.067	0.115	86.60%	13.3%	4	30
0.27		3	0.567	0.000	1.000	0.296	0.513	90.60%	56.7%	17	30
0.6		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	30	30

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

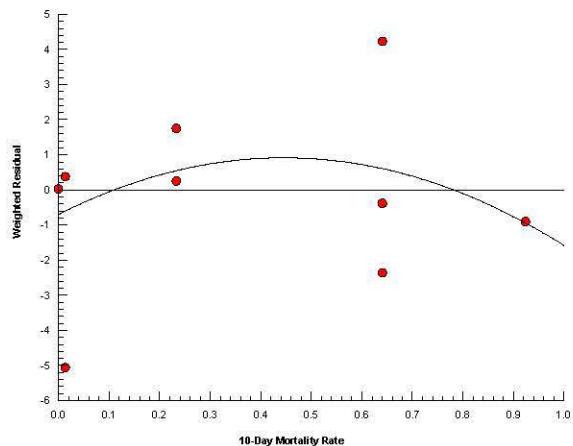
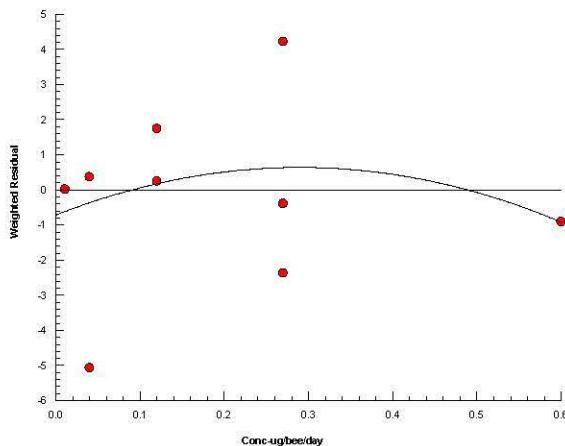
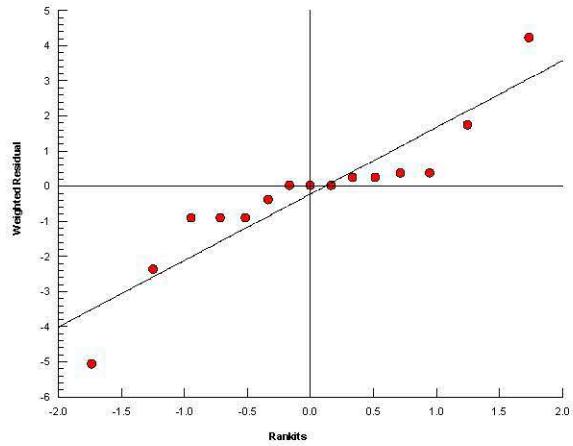
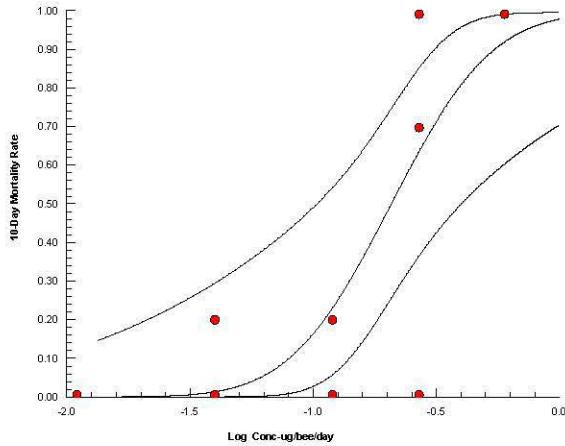
Eurofins EAG Agroscience LLC

Analysis ID: 17-1326-1333
 Analyzed: 17 Jul-19 15:57

Endpoint: 10-Day Mortality Rate
 Analysis: Linear Regression (GLM)

CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 17 Jul-19 16:11 (p 1 of 2)
 Test Code/ID: 50845001 dd / 07-3139-5452

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

Eurofins EAG Agroscience LLC

Analysis ID:	02-7253-2663	Endpoint:	Food Consumption	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 15:58	Analysis:	Nonlinear Regression (NLR)	Status Level:	1
Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
				Age:	

Non-Linear Regression Options

Model Name and Function	Weighting Function	PTBS Function	X Trans	Y Trans
3P Cum Log-Normal (Probit): $\mu = \alpha - \Phi[\log[x/\delta]/\gamma]$	Normal [$\omega=1$]	Off [$\mu^*=\mu$]	None	None

Regression Summary

Iters	Log LL	AICc	BIC	Adj R2	PMSE	Thresh	Optimize	F Stat	P-Value	Decision($\alpha:5\%$)
86	-27	61.7	62.6	0.5512	10.43%	31.2	Yes	1.41	0.2878	Non-Significant Lack of Fit

Point Estimates

Level	ug/bee/day	95% LCL	95% UCL
EC5	0.153	n/a	0.282
EC10	0.209	n/a	0.36
EC25	0.352	0.199	0.516
EC50	0.628	0.403	0.976

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
α	31.2	1.53	27.9	34.4	20.4	<1.0E-37	Significant Parameter
γ	0.857	0.378	0.0506	1.66	2.27	0.0387	Significant Parameter
δ	0.628	0.126	0.358	0.897	4.96	1.7E-04	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	14300	4780	3	211	<1.0E-37	Significant
Lack of Fit	88.7	29.6	3	1.41	0.2878	Non-Significant
Pure Error	252	21	12			
Residual	340	22.7	15			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Variance	Bartlett Equality of Variance Test	5.08	11.1	0.4057	Equal Variances
	Mod Levene Equality of Variance	1.18	4.39	0.4155	Equal Variances
Distribution	Anderson-Darling A2 Normality Test	0.715	2.49	0.0620	Normal Distribution
	Shapiro-Wilk W Normality Test	0.918	0.897	0.1197	Normal Distribution

Food Consumption Summary

Conc-ug/bee/day	Code	Count	Calculated Variate						
			Mean	Min	Max	Std Err	Std Dev	CV%	%Effect
0	N	3	28.2	26.8	30	0.935	1.62	5.73%	0.0%
0.011		3	29.8	27.1	33.8	2	3.47	11.60%	-5.68%
0.04		3	33.4	24.8	39.3	4.39	7.6	22.80%	-18.1%
0.12		3	33.7	27	39.2	3.56	6.16	18.30%	-19.1%
0.27		3	24.4	22.4	27.3	1.51	2.61	10.70%	13.8%
0.6		3	16.8	13.5	19.2	1.7	2.94	17.50%	40.5%

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

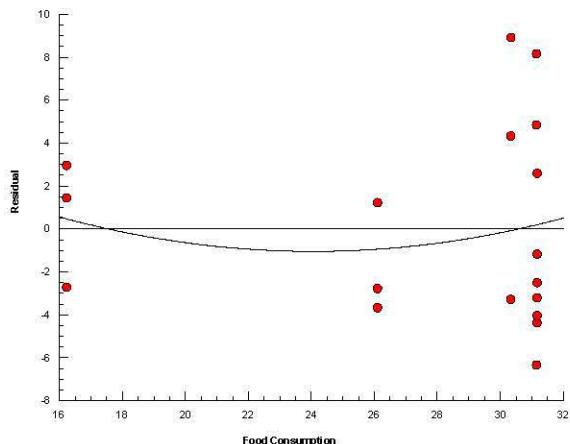
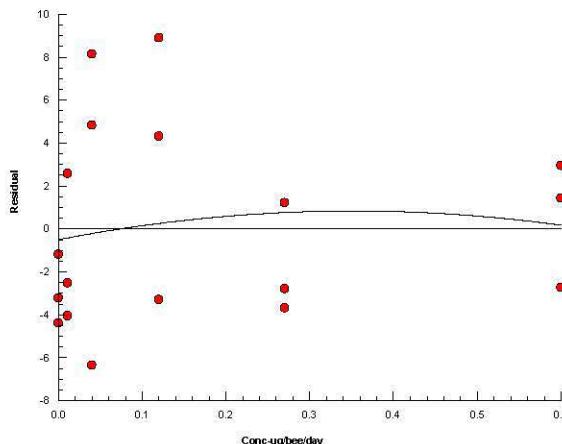
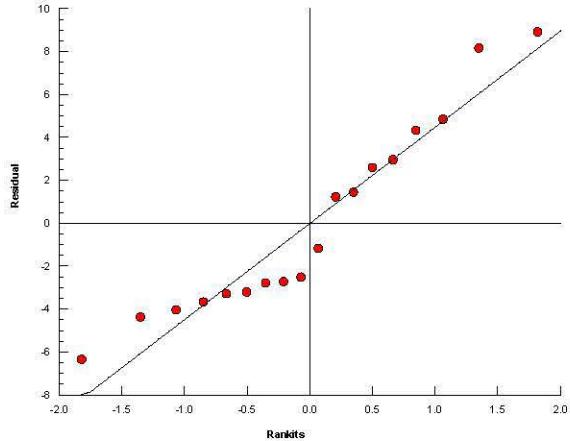
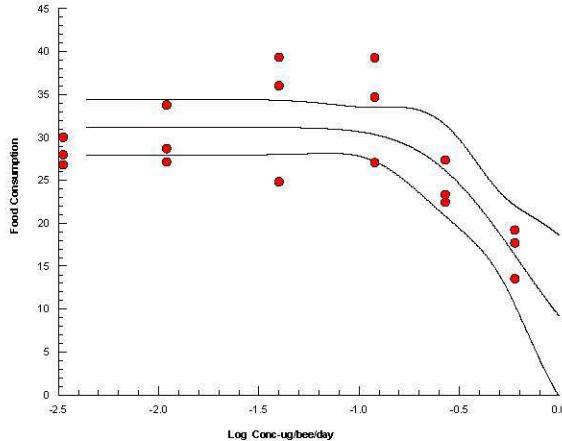
Eurofins EAG Agroscience LLC

Analysis ID: 02-7253-2663
 Analyzed: 17 Jul-19 15:58

Endpoint: Food Consumption
 Analysis: Nonlinear Regression (NLR)

CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Model: 3P Cum Log-Normal (Probit): $\mu = \alpha [1 - \Phi[\log(x/\delta)/\gamma]]$ Distribution: Normal [$\omega=1$]

CETIS Analytical Report

Report Date: 17 Jul-19 16:12 (p 1 of 1)
 Test Code/ID: 50845001 dd / 07-3139-5452

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

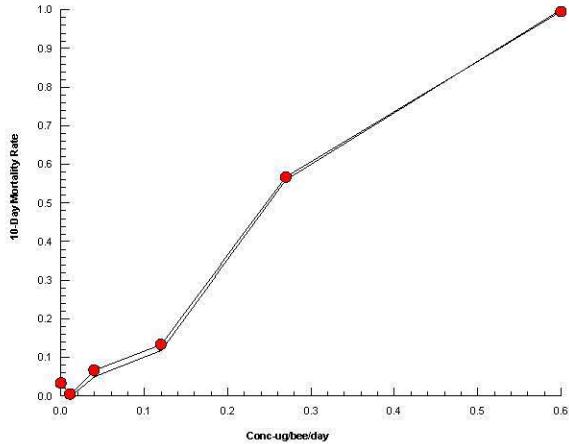
Eurofins EAG Agroscience LLC

Analysis ID:	12-8218-8541	Endpoint:	10-Day Mortality Rate	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 15:57	Analysis:	Untrimmed Spearman-Kärber	Status Level:	1
Batch ID:	16-7140-8845	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
				Age:	

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.0333	0.00%	-0.666	0.0451	0.216	0.175	0.265

10-Day Mortality Rate Summary			Calculated Variate(A/B)						Isotonic Variate		
Conc-ug/bee/day	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.033	0.000	0.100	0.058	173.00%	0.0%	1/30	0.0167	0.0%
0.011		3	0.000	0.000	0.000	0.000		-3.45%	0/30	0.0167	0.0%
0.04		3	0.067	0.000	0.200	0.115	173.00%	3.45%	2/30	0.0667	5.08%
0.12		3	0.133	0.000	0.200	0.115	86.60%	10.3%	4/30	0.133	11.9%
0.27		3	0.567	0.000	1.000	0.513	90.60%	55.2%	17/30	0.567	55.9%
0.6		3	1.000	1.000	1.000	0.000	0.00%	100.0%	30/30	1	100.0%

Graphics

CETIS Analytical Report

Report Date: 17 Jul-19 16:13 (p 1 of 2)
 Test Code/ID: 50845001 dc / 09-7178-1966

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study Eurofins EAG Agroscience LLC

Analysis ID:	04-1832-4856	Endpoint:	10-Day Mortality Rate	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 16:02	Analysis:	Linear Regression (GLM)	Status Level:	1
Batch ID:	09-1432-1139	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
				Age:	

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSE	F Stat	P-Value	Decision($\alpha:5\%$)
7	-27.1	59.2	59.6	0.895	0.394	0.999		0.594	0.6330	Non-Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
EC5	1.76	0.194	3.57
EC10	2.45	0.411	4.59
EC25	4.25	1.35	7.42
EC50	7.84	4.04	15.9

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	-2.27	0.664	-3.7	-0.834	-3.42	0.0046	Significant Parameter
Slope	2.54	0.684	1.06	4.01	3.7	0.0026	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	51300	51300	1	14600	<1.0E-37	Significant
Lack of Fit	6.91	2.3	3	0.594	0.6331	Non-Significant
Pure Error	38.8	3.88	10			
Residual	45.7	3.51	13			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	44.4	22.4	2.7E-05	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	45.7	22.4	1.6E-05	Significant Heterogeneity
Variance	Mod Levene Equality of Variance	1.41	5.19	0.3517	Equal Variances
	Anderson-Darling A2 Normality Test	1.09	2.49	0.0076	Non-Normal Distribution
Distribution	Shapiro-Wilk W Normality Test	0.88	0.882	0.0472	Non-Normal Distribution
	Tarone C(α) Binomial Overdispersion	7.94	1.64	<1.0E-37	Significant Overdispersion

10-Day Mortality Rate Summary Calculated Variate(A/B)

Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.38		3	0.000	0.000	0.000	0.000	0.000	0.0%	0	30	
1.2		3	0.067	0.000	0.200	0.067	0.115	173.00%	6.67%	2	30
3.6		3	0.133	0.000	0.200	0.067	0.115	86.60%	13.3%	4	30
11		3	0.567	0.000	1.000	0.296	0.513	90.60%	56.7%	17	30
33		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	30	30

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

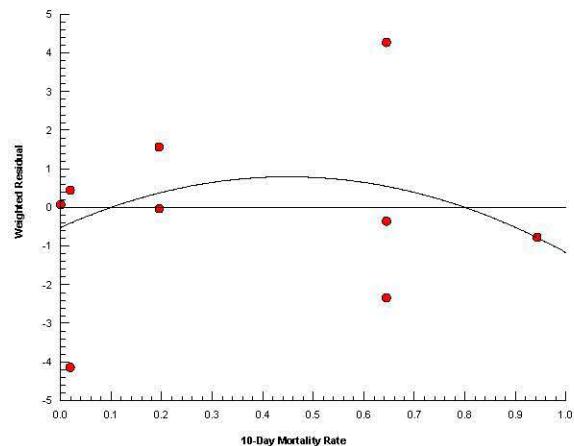
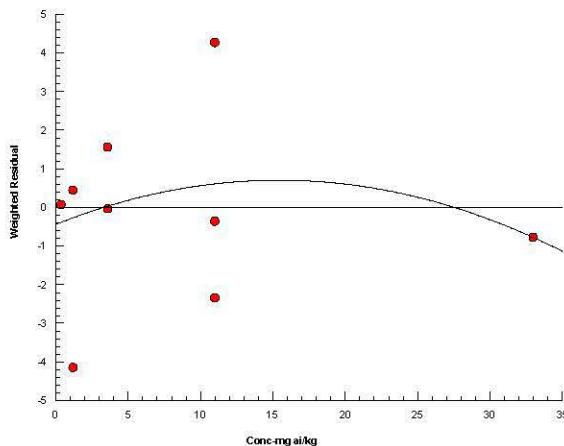
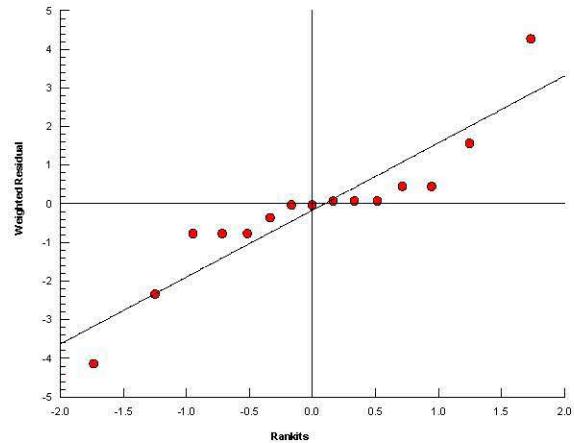
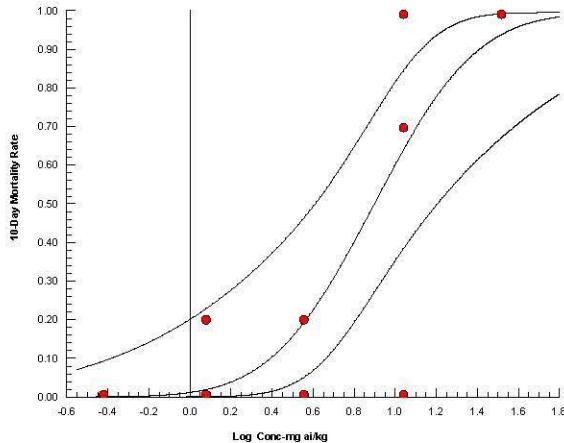
Eurofins EAG Agroscience LLC

Analysis ID: 04-1832-4856
 Analyzed: 17 Jul-19 16:02

Endpoint: 10-Day Mortality Rate
 Analysis: Linear Regression (GLM)

CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 17 Jul-19 16:14 (p 1 of 2)
 Test Code/ID: 50845001 dc / 09-7178-1966

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study **Eurofins EAG Agroscience LLC**

Analysis ID:	14-1726-5355	Endpoint:	Food Consumption	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 16:03	Analysis:	Nonlinear Regression (NLR)	Status Level:	1

Batch ID:	09-1432-1139	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:
Test Length:	10d 0h	Taxon:		Source: Eurofins Agroscience Servi Age:

Non-Linear Regression Options

Model Name and Function	Weighting Function	PTBS Function	X Trans	Y Trans
3P Cum Log-Normal (Probit): $\mu = \alpha - \Phi[\log[x/\delta]/\gamma]$	Normal [$\omega=1$]	Off [$\mu^*=\mu$]	None	None

Regression Summary

Iters	Log LL	AICc	BIC	Adj R2	PMSD	Thresh	Optimize	F Stat	P-Value	Decision($\alpha:5\%$)
100	-27	61.7	62.6	0.5505		31.2	Yes	1.42	0.2855	Non-Significant Lack of Fit

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
α	31.2	1.55	27.9	34.5	20.2	<1.0E-37	Significant Parameter
γ	1.17	0.522	0.0567	2.28	2.24	0.0407	Significant Parameter
δ	35	9.61	14.5	55.5	3.64	0.0024	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	14300	4780	3	210	<1.0E-37	Significant
Lack of Fit	89.3	29.8	3	1.42	0.2855	Non-Significant
Pure Error	252	21	12			
Residual	341	22.7	15			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Variance	Bartlett Equality of Variance Test	5.08	11.1	0.4057	Equal Variances
	Mod Levene Equality of Variance	1.18	4.39	0.4155	Equal Variances
Distribution	Anderson-Darling A2 Normality Test	0.718	2.49	0.0609	Normal Distribution
	Shapiro-Wilk W Normality Test	0.917	0.897	0.1141	Normal Distribution

Food Consumption Summary			Calculated Variate						
Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	% Effect
0	N	3	28.2	26.8	30	0.935	1.62	5.73%	0.0%
0.38		3	29.8	27.1	33.8	2	3.47	11.60%	-5.68%
1.2		3	33.4	24.8	39.3	4.39	7.6	22.80%	-18.1%
3.6		3	33.7	27	39.2	3.56	6.16	18.30%	-19.1%
11		3	24.4	22.4	27.3	1.51	2.61	10.70%	13.8%
33		3	16.8	13.5	19.2	1.7	2.94	17.50%	40.5%

Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study

Eurofins EAG Agroscience LLC

Analysis ID: 14-1726-5355

Endpoint: Food Consumption

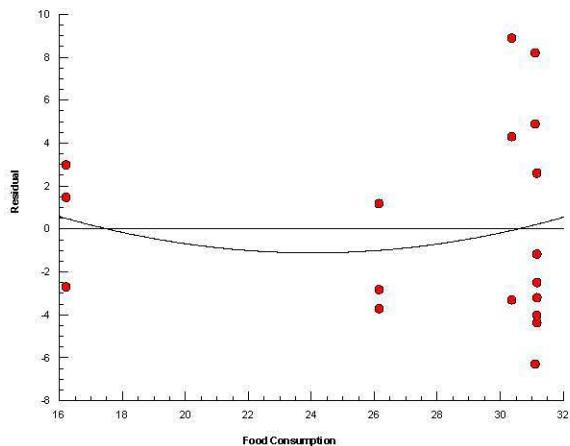
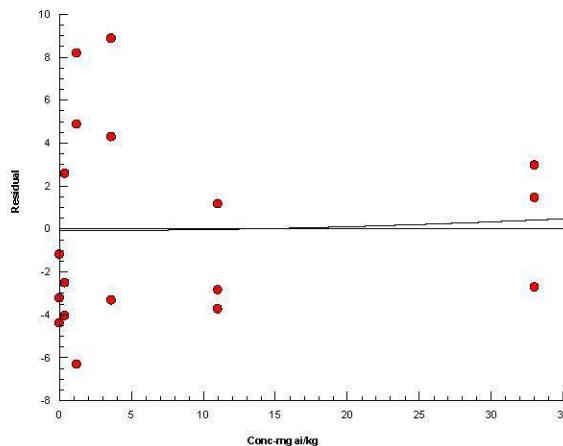
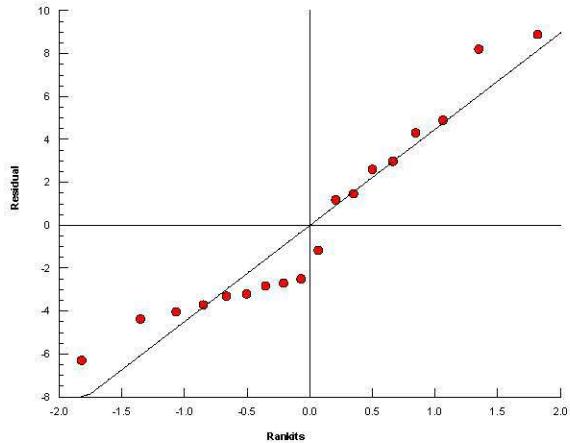
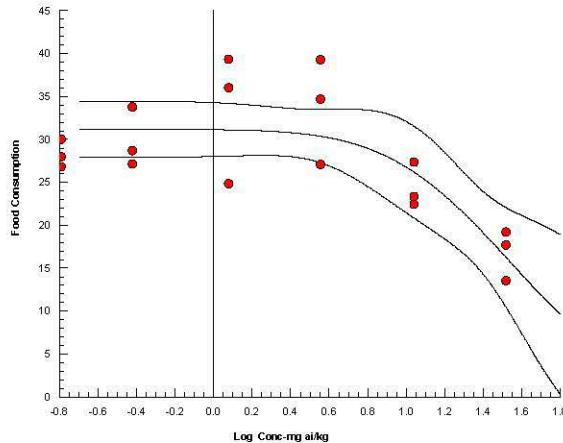
CETIS Version: CETISv1.9.5

Analyzed: 17 Jul-19 16:03

Analysis: Nonlinear Regression (NLR)

Status Level: 1

Graphics

Model: 3P Cum Log-Normal (Probit): $\mu = \alpha [1 - \Phi[\log(x/\delta)/\gamma]]$ Distribution: Normal [$\omega=1$]

CETIS Analytical ReportReport Date: 17 Jul-19 16:14 (p 1 of 1)
Test Code/ID: 50845001 dc / 09-7178-1966**Special Study Honey bee Adult Chronic Oral Toxicity, 10-day Study****Eurofins EAG Agroscience LLC**

Analysis ID:	21-3477-9190	Endpoint:	10-Day Mortality Rate	CETIS Version:	CETISv1.9.5
Analyzed:	17 Jul-19 16:02	Analysis:	Untrimmed Spearman-Kärber	Status Level:	1
Batch ID:	09-1432-1139	Test Type:	2014 Honeybee Adult Chron Oral	Analyst:	
Start Date:	19 Feb-19	Protocol:	Honeybee Adult Chronic Oral Toxicity, 10-d	Diluent:	
Ending Date:	01 Mar-19	Species:	Apis mellifera	Brine:	
Test Length:	10d 0h	Taxon:		Source:	Eurofins Agroscience Servi
				Age:	

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.0333	0.00%	0.929	0.0556	8.49	6.57	11

10-Day Mortality Rate Summary			Calculated Variate(A/B)						Isotonic Variate		
Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.033	0.000	0.100	0.058	173.00%	0.0%	1/30	0.0167	0.0%
0.38		3	0.000	0.000	0.000	0.000		-3.45%	0/30	0.0167	0.0%
1.2		3	0.067	0.000	0.200	0.115	173.00%	3.45%	2/30	0.0667	5.08%
3.6		3	0.133	0.000	0.200	0.115	86.60%	10.3%	4/30	0.133	11.9%
11		3	0.567	0.000	1.000	0.513	90.60%	55.2%	17/30	0.567	55.9%
33		3	1.000	1.000	1.000	0.000	0.00%	100.0%	30/30	1	100.0%

Graphics